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TITLE: Blocking Internalization of Phosphatidylethanolamine at Cleavage Furrow of Mitosis as a Novel Mechanism of Anti-Breast-Cancer Strategy

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13. ABSTRACT (Maximum 200 Words)

During the formation of cleavage furrow of mitosis, phosphatidylethanolamine (PE) flips from inner leaflet of the plasma membrane to the outer leaflet specifically in the furrow region near the contractile ring. Immediately after the contractile ring separates the two daughter cells, PE returns from outer leaflet to inner leaflet. This transient movement of PE during cytokinesis is essential because blockage of this PE movement results in a failure of mitosis and leads to cell death. Cinnamycin produced by Streptoverticillium griseoverticillatum targets specifically to PE on cell surface at the cleavage furrow of mitotic cells but not the non-dividing cells. This proposal is to test if cinnamycin is a better anti-tumor drug for treatment of breast cancers because of several advantages: 1) Cinnamycin only targets proliferating cells but has no effect on non-proliferating cells. 2) The anti-proliferation activity doesn't require cinnamycin to enter the cells. 3) Cinnamycin doesn't have to suffer the effect of multi-drug resistance mechanism or cellular metabolism. Because cinnamycin is no longer available commercially, we had to devise production procedures and to purify this compound in our own lab. Thus, completion of this proposal would require longer time than that was originally proposed.

14. SUBJECT TERMS
Breast cancer; cinnamycin, anti-cancer therapy, mouse model

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Final Report

Introduction.....

During the formation of cleavage furrow of mitosis, phosphatidylethanolamine (PE) flips from inner leaflet of the plasma membrane to the outer leaflet specifically in the furrow region near the contractile ring. Immediately after the contractile ring separates the two daughter cells, PE returns from outer leaflet to inner leaflet. This transient movement of PE during cytokinesis is essential because blockage of this PE movement results in a failure of mitosis and leads to cell death. Cinnamycin produced by Streptoverticillium griseoverticillatum targets specifically to PE on cell surface at the cleavage furrow of mitotic cells but not the non-dividing cells. This proposal is to test if cinnamycin is a better anti-tumor drug for treatment of mammary cancer models in mice.

Body.....

Because cinnamycin is no longer available commercially, we had to devise production procedures and to purify this compound in our own lab. Thus, completion of this proposal would require longer time than that was originally proposed. In the initial funding period, we have performed extensive literature search for commercial source of cinnamycin suppliers. However, none of the previous suppliers continues to sell this compound. We proceeded to contact several academic investigators who have published using this compound. All these investigators have stopped to use this compound and no longer have it in their possession. Thus we have decided to produce and purify this compound in our own lab.

Key Research Accomplishments.....

During the residual funding period since last report, we have attempted to produce and isolate cinnamycin from cell culture of bacterium Streptoverticillium griseoverticillatum.

Reportable Outcomes.....

None.

Conclusions.....

Cinnamycin is an old compound that is no longer produced by any commercial source or by academic entity. Thus our goal to test its anti-breast cancer effect could not be performed as we originally planned. The emphasis then changed to production of cinnamycin in our own lab. Although several attempts were made to purify the peptide, we were not able to isolate enough peptide to perform any test in cell culture experiment and animal experiments in the proposed budget and time frame. However, we will continue to isolate cinnamycin in our lab as well as to search collaboration partners who had experience in isolation of the peptide even after this funding is over. Once enough cinnamycin is obtained, we will seek other funding resources to perform tests in animals.

References.....

None.

Appendices.....

None